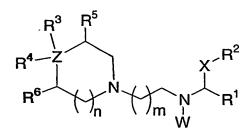
WHAT IS CLAIMED IS:

1. A compound of the formula I:



I

5 wherein:

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X is selected from the group consisting of:

-NR10-, -O-, -CH2O-, -CONR10-, -NR10CO-, -CO2-, -OCO-,

-CH2(NR10)CO-, -N(COR10)-, -CH2N(COR10)-, phenyl, and

10 C₃₋₆ cycloalkyl,

where R^{10} is independently selected from: hydrogen, C_{1-6} alkyl, benzyl, phenyl, and

C₁₋₆ alkyl-C₃₋₆ cycloalkyl,

which is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, C_{1-3} alkyl,

C₁-3alkoxy and trifluoromethyl;

W is selected from:

hydrogen and C₁₋₆ alkyl, which is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, C₁₋₃ alkoxy and trifluoromethyl;

Z is selected from:

C, N, and -O-, wherein when Z is N, then R^4 is absent, and when W is -O-, then both R^3 and R^4 are absent;

n is an integer selected from 0, 1, 2, 3 and 4;

n is an integer selected from 1, 2, 3 and 4;

R¹ is selected from:

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hydrogen, -C0-6alkyl-, -(C0-6alkyl)-alkenyl-,

-(C0-6alkyl)-C3-6cycloalkyl, -(C0-6alkyl)-phenyl,

and -(C0-6alkyl)-heterocycle,

where the alkyl is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋3alkyl,
 - (d) trifluoromethyl, and
 - (e) -C₁-3alkyl,

and where the phenyl and the heterocycle is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- 15 (a) halo,
 - (b) hydroxy; alkoxy
 - (c) amino; acylamino; sulfonylamino; alkoxycarbonylamino
 - (d) carboxylic acid; carbamide; sulfonamide
- 20 or wherein W and R¹ may be joined together to form a ring by a group selected from:

-(C1-6alkyl)-, -C0-6alkyl-Y-(C1-6alkyl)-, and

-(C₀-6alkyl)-Y-(C₀-6alkyl)-(C₃-7cycloalkyl)-(C₀-6alkyl),

where Y is selected from:

a single bond, -O-, -S-, -SO-, -SO₂-, and -NR¹⁰-,

and where the alkyl and the cycloalkyl are unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl, and
- (d) trifluoromethyl,
- (e) C₁₋₃alkyl,
- (f) -O-C₁₋₃alkyl,
- (g) -CO₂R⁹, wherein R⁹ is independently selected from: hydrogen, C₁₋₆ alkyl, C₅₋₆ cycloalkyl, benzyl or phenyl, which is unsubstituted or

substituted with 1-3 substituents where the substituents are independently selected from: halo, C₁₋₃alkyl, C₁₋₃alkoxy and trifluoromethyl,

- (h) -CN,
- (i) -NR9R10,
- (j) $-NR^9COR^{10}$,
- (k) -NR9SO₂R¹⁰, and
- (1) $-CONR^9R^{10}$;

R² is selected from:

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10 (C₀₋₆alkyl)-phenyl and (C₀₋₆alkyl)-heterocycle,

where the alkyl is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl,
- (d) trifluoromethyl, and
- (e) -C₁-3alkyl,

and where the phenyl and the heterocycle is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- 20 (a) halo,
 - (b) trifluoromethyl,
 - (c) trifluoromethoxy,
 - (d) hydroxy,
 - (e) C₁₋₆alkyl,
 - (f) C₃₋₇cycloalkyl,
 - (g) -O-C₁₋₆alkyl,
 - (h) -O-C3-7cycloalkyl,
 - (i) -SCF₃,
 - (j) -S-C₁₋₆alkyl,
 - (k) -SO₂-C₁₋₆alkyl,
 - (l) phenyl,
 - (m) heterocycle,
 - (n) $-CO_2R^9$,
 - (o) -CN,

 $-NR^9R^{10}$ (p) -NR9-SO2-R10, (q) -SO₂-NR⁹R¹⁰, and (r) -CONR9R10; (s) 5 R³ is -(C₀₋₆alkyl)-phenyl, where the alkyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from: (a) halo, 10 (b) hydroxy, -O-C₁₋₃alkyl, and (c) (d) trifluoromethyl, and where the phenyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from: 15 (a) halo, (b) trifluoromethyl, (c) hydroxy, (d) C₁-3alkyl, -O-C₁₋₃alkyl, (e) 20 $-CO_2R^9$, (f) -CN, (g) -NR9R10, and (h) -CONR9R10; (i) R⁴ is selected from: 25 hydrogen, (a) (b) hydroxy, (c) C₁-6alkyl, (d) C₁-6alkyl-hydroxy, 30 (e) -O-C₁₋₃alkyl, (f) $-CO_2R^9$, -CONR9R10, and (g)

(h)

-CN;

or where R³ and R⁴ may be joined together to form a ring which is selected from: (a) 1H-indene, (b) 2,3-dihydro-1H-indene, 2,3-dihydro-benzofuran, (c) 1,3-dihydro-isobenzofuran, (d) 5 2,3-dihydro-benzothiofuran, and (e) 1,3-dihydro-isobenzothiofuran, **(f)** or where R³ and R⁵ or R⁴ and R⁶ may be joined together to form a ring which is phenyl, wherein the ring is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from: 10 halo, (a) trifluoromethyl, (b) hydroxy, (c) C₁₋₃alkyl, (d) -O-C₁₋₃alkyl, 15 (e) $-CO_2R^9$, (f) -CN, (g) -NR9R10, and (h) -CONR9R10; (i) 20 R⁵ and R⁶ are independently selected from: hydrogen, (a) hydroxy, (b) C₁-6alkyl, (c) C₁₋₆alkyl-hydroxy, 25 (d) -O-C₁₋₃alkyl, (e) oxo, and (f) (g) halo;

2. The compound of Claim 1 of the formula Ia:

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and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

$$R^3$$
 R_4
 R^5
 R_4
 R^6
 R^6
 R^6
 R^6
 R^6
 R^6
 R^6
 R^7
 R^8
 R^8
 R^8
 R^8
 R^8

Ia

and pharmaceutically acceptable salts and individual diastereomers thereof.

5 3. The compound of Claim 1 of the formula Ib:

$$R_4$$
 R_4
 R_4

Ιb

10 wherein:

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the dashed line represents a single or a double bond;

R¹¹ is selected from:

(a) hydrogen

(b) C₁₋₆alkyl

(c) hydroxy,

(d) -O-C₁₋₃alkyl

(e) -Phenyl and heterocycle,

(f) $-CO_2R^9$,

(g) -CN,

(h) $-NR^9R^{10}$, and

(i) $-CONR^9R^{10}$;

R¹² is selected from:

	(a)	hydrogen,	
	(b)	hydroxy,	
	(c)	C ₁₋₆ alkyl,	
	(d)	C ₁₋₆ alkyl-hydroxy,	
5	(e)	-O-C ₁₋ 3alkyl,	
	(f)	-CO ₂ R ⁹ ,	
	(g)	-CONR ⁹ R ¹⁰ , and	
	(h)	-CN;	
or where R^{11} and R^{12} may be joined together to form a		12 may be joined together to form a ring which is selected from:	
	(a)	benzene,	
	(b)	furan,	
	(c)	thiophene,	
	(d)	thiazole,	
15	(e)	C3_6cycloalkyl	
	wherein the ring is unsubstituted or substituted with 1-7 substituents where the		
	subst	ituents are independently selected from:	
	(a)	halo,	
	(b)	trifluoromethyl,	
20	(c)	hydroxy,	
	(d)	C ₁₋₃ alkyl,	
	(e)	-O-C ₁₋ 3alkyl,	
	(f)	-CO ₂ R ⁹ ,	
	(g)	-CN,	
25	(h)	-NR9R10, and	
	(i)	-CONR ⁹ R ¹⁰ ;	

and pharmaceutically acceptable salts and individual diastereomers thereof.

4. The compound of Claim 3 of the formula Id:

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Id

and pharmaceutically acceptable salts and individual diastereomers thereof.

5. The compound of Claim 3 of the formula Ie:

$$R_4$$
 R_4
 R_4

wherein $\,R^{13}$ is independently selected from:

10 (a) hydrogen,

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(b) halo,

(c) trifluoromethyl,

(d) fused C₁₋₃cycloalkyl

(e) C₁₋₃alkyl,

(f) -O-C₁-3alkyl,

(g) -CO₂H,

(h) -CO₂C₁₋₃alkyl, and

(i) -CN;

and pharmaceutically acceptable salts and individual diastereomers thereof.

6. The compound of Claim 3 of the formula If:

$$R_4$$
 N
 N
 R^3
 N
 R^2

If

and pharmaceutically acceptable salts and individual diastereomers thereof.

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7. The compound of Claim 1 of the formula II:

П

- wherein R¹⁴, R¹⁵, R¹⁶ are independently selected from:
 - (a) hydrogen,
 - (b) -C₁-6alkyl
 - (c) -C₁-6cycloalkyl
 - (d) -C₁₋₆alkyl-phenyl
 - (e) -C₁-6alkyl-heterocylcle
 - (f) -C₁-6alkyl-C₃-6cycloakyl
 - (g) C₁-6alkyl O-C₁-6alkyl,

and pharmaceutically acceptable salts and individual diastereomers thereof.

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8. The compound of Claim 1 of the formula IIa:

Па

and pharmaceutically acceptable salts and individual diastereomers thereof.

9. The compound of Claim 1 of the formula IIb:

 Πb

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and pharmaceutically acceptable salts and individual diastereomers thereof.

10. The compound of Claim 1 of the formula IIc:

Пc

and pharmaceutically acceptable salts and individual diastereomers thereof.

11. The compound of Claim 1 of the formula:

$$R^3$$
 N
 N
 R^2
 R^{12}

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wherein:

the dashed line represents a single or a double bond,

- 20 R¹¹ and R¹² are hydrogen or where R¹¹ and R¹² may be joined together to form a ring which is selected from:
 - (a) benzene,

PCT/US2003/033980

(b) heterocycle

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(c) C3-6cyclalkyl

and pharmaceutically acceptable salts and individual diastereomers thereof.

12. The compound of Claim 1 of the formula:

$$R^3$$
 N
 N
 R^1

$$R^3$$
 R^4
 N
 N
 N
 N

$$R^3$$
 X
 R^2
 X
 X

and pharmaceutically acceptable salts and individual diastereomers thereof.

13. The compound of Claim 1 wherein W is hydrogen or -CH2-.

- 14. The compound of Claim 1 wherein X is -CONH-, phenyl or heterocycle.
- 15. The compound of Claim 1 wherein Z is -C- or -N-.
- 16. The compound of Claim 1 wherein n is 0 and 1.

- 17. The compound of Claim 1 wherein m is 1.
- 18. The compound of Claim 1 wherein heterocycle is selected from: furanyl, imidazolyl, oxadiazolyl, oxazolyl, pyrazolyl, pyrazinyl, pyridyl, pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, thiazolyl, and triazolyl, and N-oxides thereof.
 - 19. The compound of Claim 1 wherein -C₁-6alkyl, -C₀-6alkyl-O-C₁-6alkyl-, -C₀-6alkyl-S-C₁-6alkyl-, and -(C₀-6alkyl)-(C₃-7cycloalkyl)-(C₀-6alkyl),

where the alkyl and the cycloalkyl are unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) $-O-C_{1-3}$ alkyl,
- (d) trifluoromethyl,
 - (f) C₁₋₃alkyl,
 - (g) -O-C₁₋₃alkyl,
 - (h) -CO₂R⁹, wherein R⁹ is independently selected from: hydrogen, C₁₋₆ alkyl, C₅₋₆ cycloalkyl, benzyl or phenyl, which is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, C₁₋₃alkyl, C₁₋₃alkoxy and trifluoromethyl,
 - (i) -CN,
 - (j) -NR9R10, and
 - (k) $-CONR^9R^{10}$.

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- 20. The compound of Claim 1 wherein R¹ is selected from:
- -C₁-6alkyl, which is unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from:
 - (a) halo,

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- (b) hydroxy,
- (c) -O-C₁₋₃alkyl, and
- (d) trifluoromethyl,
- (2) -C₀₋₆alkyl-O-C₁₋₆alkyl-, which is unsubstituted or substituted with 1-6 substituents where the substituents are independently selected from:

		(a) halo, and	
		(b) trifluoromethyl,	
(3) -C ₀₋₆ alkyl-S-C ₁₋₆ alkyl-, which is un		-C ₀₋₆ alkyl-S-C ₁₋₆ alkyl-, which is unsubstituted or substituted with 1-6	
		substituents where the substituents are independently selected from:	
5		(a) halo, and	
		(b) trifluoromethyl,	
	(4)	-(C3-5cycloalkyl)-(C0-6alkyl), which is unsubstituted or substituted with 1	
		substituents where the substituents are independently selected from:	
		(a) halo,	
10		(b) hydroxy,	
		(c) -O-C ₁₋₃ alkyl, and	
		(d) trifluoromethyl.	
		21. The compound of Claim 1 wherein R ¹ is selected from:	
15	(1)	-CH3,	
	(2)	-CH ₂ CH ₃ ,	
	(3)	-CH(CH ₃) ₂ ,	
	(4)	-CH ₂ CH ₂ CH ₃ ,	
	(5)	-CH ₂ CH(CH ₃) ₂ ,	
20	(6)	-cyclopropyl,	
	(7)	-cyclobutyl,	
	(8)	-cyclopentyl,	
	(9)	-CH ₂ -cyclopropyl,	
	(10)	-CH ₂ -cyclobutyl,	
25	(11)	-CH ₂ -cyclopentyl,	
	(12)	-CH ₂ OH,	
	(13)	-C(CH ₃) ₂ (OH),	
	(14)	-C(CH ₂ OH)(CH ₃) ₂ ,	
	(15)	-(OH)cyclobutyl,	
30	(16)	-(OH)cyclopentyl,	
•	(17)	-C(CH ₃) ₂ (NHCOCH ₃),	
	(18)	-C(CO ₂ H)(CH ₃) ₂ ,	
	(19)	-O-CH3,	
	(20)	-O-cyclopentyl.	

	(22) -S-CH ₃ ,	•	
	(23) -S-CF ₃ ,	-S-CF ₃ ,	
	(24) -SO ₂ -CH ₃ ,		
5 (25) -S-CH(CH ₃) ₂ ,		,	
	(26) -SO ₂ -CH(CH	3)2, and	
	(27) -NH-SO ₂ -CH	3.	
	22. The co	empound of Claim 1 wherein R ² is selected from	
10	-(C ₀₋₄ alkyl)-phenyl and -(C ₀	_4alkyl)-heterocycle,	
where heterocycle is selected from:		selected from:	
		zolyl, oxadiazolyl, oxazolyl, pyrazolyl, pyrazinyl, pyridyl,	
	pyridazinyl, p	yrimidyl, pyrrolyl, thiadiazolyl, thiazolyl, thienyl, and triazolyl, and	
	N-oxides ther	eof,	
where the alkyl is unsubstituted or substituted with 1-7 substituents where the		substituted or substituted with 1-7 substituents where the	
	substituents a	re independently selected from:	
	(a) halo,		
	(b) hydro		
	(c) -O-C ₁	-3alkyl, and	
20	· ·	romethyl,	
	and where the phenyl or heterocycle is unsubstituted or substituted with 1-5 substitu		
	where the substituents are independently selected from:		
	(a) halo,		
	(b) trifluo	promethyl,	
25	(c) trifluo	promethoxy,	
	(d) hydro		
	(e) C ₁₋₃		
	* *	₁₋₃ alkyl,	
	(g) -CO ₂	•	
30	• •	-3alkyl,	
	• • • • • • • • • • • • • • • • • • • •	-C ₁₋ 3alkyl,	
	(j) -SCF		
	(k) -CO ₂	R ⁹ ,	

(21) -O-CH(CH₃)₂,

(1) $-NR^9R^{10}$,

- (m) $-NR9-SO_2-R_{10}$,
- (n) $-SO_2-NR^9R^{10}$, and
- (o) $-CONR^9R^{10}$.

5 23. The compound of Claim 1 wherein R² is selected from -(C₀₋₄alkyl)-phenyl and -(C₀₋₄alkyl)-heterocycle,

where heterocycle is selected from: pyridyl, pyridazinyl, and N-oxides thereof, where the alkyl is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

10 (a) halo,

- (b) hydroxy,
- (c) -O-C₁-3alkyl, and
- (d) trifluoromethyl,

and where the phenyl or heterocycle is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) trifluoromethoxy,
- (d) hydroxy,
- 20 (e) C₁₋₃alkyl,
 - (f) -O-C₁₋₃alkyl,
 - (g) -CO₂-C₁-3alkyl,
 - (h) -CO₂H,
 - (i) -S-C₁-3alkyl,
 - (j) -SO₂-C₁-3alkyl,
 - (k) -SCF₃,
 - (1) -NH2,
 - (m) -NH-SO₂-C₁₋₃alkyl, and
 - (n) -SO₂-NH₂.

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24. The compound of Claim 1 wherein R² is selected from -CH₂-phenyl and -CH₂-heterocycle,

where heterocycle is selected from: pyridyl, pyridazinyl, and N-oxides thereof,

and where the phenyl or heterocycle is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- 5 (c) trifluoromethoxy,
 - (d) hydroxy,
 - (e) C₁₋₃alkyl,
 - (f) -O-C₁-3alkyl,
 - (g) -CO₂-C₁-3alkyl,
- 10 (h) -CO₂H,
 - (i) -S-C₁₋₃alkyl,
 - (j) -SO₂-C₁₋₃alkyl,
 - (k) -SCF₃,
 - (l) -NH₂,
- 15 (m) -NH-SO₂-C₁-3alkyl, and
 - (n) $-SO_2-NH_2$.
 - 25. The compound of Claim 1 wherein R² is selected from:
 - (1) -CH₂-(phenyl),
- 20 (2) -CH₂-(4-bromophenyl),
 - (3) -CH₂-(3-chlorophenyl),
 - (4) -CH2-(3,5-difluorophenyl),
 - (5) -CH2-((2-trifluoromethyl)phenyl),
 - (6) -CH2-((3-trifluoromethyl)phenyl),
- 25 (7) -CH₂-((4-trifluoromethyl)phenyl),
 - (8) -CH2-((3-trifluoromethoxy)phenyl),
 - (9) -CH2-((3-trifluoromethylthio)phenyl),
 - (10) -CH2-((3-trifluoromethoxy-5-thiomethyl)phenyl),
 - (11) -CH2-((3-trifluoromethoxy-5-methoxy)phenyl),
- 30 (12) -CH₂-((3-trifluoromethoxy-5-methanesulfonyl)phenyl),
 - (13) -CH2-((3-trifluoromethoxy-5-amino)phenyl),
 - (14) -CH2-((3-trifluoromethoxy-5-aminomethanesulfonyl)phenyl),
 - (15) -CH2-((3-trifluoromethoxy-5-sulfonylamino)phenyl),
 - (16) -CH2-((3,5-bis-trifluoromethyl)phenyl),

(17)-CH2-((3-fluoro-5-trifluoromethyl)phenyl), (18)-CH(CH₃)-((3,5-bis-trifluoromethyl)phenyl), -C(CH₃)₂-((3,5-bis-trifluoromethyl)phenyl), (19)(20)-CH2-(4-(2-trifluoromethyl)pyridyl), 5 -CH2-(5-(3-trifluoromethyl)pyridyl), (21) (22)-CH2-(5-(3-trifluoromethyl)pyridazinyl), (23)-CH2-(4-(2-trifluoromethyl)pyridyl-N-oxide), and -CH2-(5-(3-trifluoromethyl)pyridyl-N-oxide). (24)10 26. The compound of Claim 1 wherein R³ is hydrogen and phenyl, where the phenyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from: (a) halo, (b) trifluoromethyl, 15 (c) hydroxy, (d) C₁-3alkyl, (e) -O-C1-3alkyl, **(f)** $-CO_2R^9$, -CN, (g) 20 -NR9R10, and (h) -CONR9R10. (i) 27. The compound of Claim 1 wherein R³ is hydrogen and phenyl, where the phenyl is unsubstituted or substituted with 1-3 substituents where the substituents are 25 independently selected from: halo, (a) (c) hydroxy, (d) C₁-3alkyl, -O-C1-3alkyl, and (e) 30 $-CO_2R^9$. (f)

28. The compound of Claim 1 wherein \mathbb{R}^3 is phenyl, or para-fluorophenyl.

29. The compound of Claim 1 wherein R⁴ is selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) -CO₂H,
- (d) -CO₂C₁₋₆alkyl, and
- (e) -CN.
- 30. The compound of Claim 1 wherein R⁵ and R⁶ are independently selected

from:

- (a) hydrogen,
 - (b) hydroxy,
 - (c) -CH₃,
 - (d) -O-CH3, and
 - (e) oxo.

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- 31. A compound which is selected from the group consisting of the title compounds of the Examples, and pharmaceutically acceptable salts and individual diastereomers thereof.
- 20 32. A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.
 - 33. A method for modulation of chemokine receptor activity in a mammal in need thereof which comprises the administration of an effective amount of the compound of Claim 1.
 - 34. A method for treating, ameliorating or controlling an inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

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35. A method for reducing the risk of an inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

36. A method for treating, ameliorating or controlling rheumatoid arthritis which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.